

Comments of the Network of Coordinating Centers for Clinical Trials (KKS-Network e.V.), Germany

on the **Good Lay Summary Practice**

The Network of Coordinating Centers for Clinical Trials (KKS-Network) represents the majority of academic clinical trial units in Germany. We appreciate the Good Lay Summary Practice Document as an important overview of regulations, best practices, and general considerations regarding the lay summary. The document not only summarizes the current regulatory and literature status, but it also describes for the first time a practical step-wise approach for the development of the lay summary and gives important information how to implement the lay summary within the trial project. Several incorporated tables, especially e.g. wording, give direct and practical support for the lay summary development.

Main points to consider

1. The KKS-Network e.V. suggests having a clearer discrimination in the Good Lay Summary Practice between the mandatory requirements and the additional options and recommendations. As the intention of the EU CTR is to simplify and harmonize the administrative provisions governing clinical trials in the union (EU CTR (4)), it would be important to provide exact and clear instructions about the mandatory minimal requirements for lay summaries in contrast to the additional described options.

Line 145-149

“The GLSP includes a combination of legal obligations enforced by the EU CTR and recommendations based on experience across the stakeholders involved in the Roadmap Initiative. As a general principle, the use of the word “should” in this document refers to optional recommendations (anchored in ethical obligations and best practices), whereas use of the word “must” refers to legal requirements, as laid out in the EU CTR.”

This very important explanation should be given in an info box and highlighted with colour to make sure that every reader is aware of this terminology.

In addition to that, it would help to identify essential requirements in contrast to additional possible options throughout the whole document (colour coded).

2. The Good Lay Summary Practice states that the described lay summary approaches may differ for academic clinical trials. However, the KKS-Network e.V. does not see any differences in the regulatory requirements or conduct of clinical trials in the academic setting as compared to clinical trials with a commercial sponsor.

Line 235-237

*“LS development approaches may differ according to the **type of sponsor (commercial or academic)** and may be adapted depending on available resources and the volume of clinical trials undertaken.”*

We therefore suggest to either delete the differentiation between commercial and academic sponsor, or to add an explanation why there should be differences in the lay summary development.

3. The Good Lay Summary Practice gives recommendations about the involvement of patients in the development of the lay summary. Since discussions of guidelines for active patient involvement in planning and designing clinical trials are currently ongoing in Germany and to avoid any confusion, KKS-Network would appreciate a clear discrimination between possible roles of the patients in the development of the lay summary and the patient involvement in other aspects of clinical trials. Especially in the description of the patient involvement of the planning phase, these two intermingle, as shown in the following phrases:

Line 343 ff: *“Consultation regarding the planning, identification and prioritisation of patient-relevant outcomes and endpoints.”*

We suggest changing this sentence in the following way:

Consultation regarding the ~~planning~~, identification and prioritisation of patient-relevant outcomes and endpoints **for the LS**.

Line 353 ff *Figure 2.1.: Patient involvement during LS Phases*

“... Define patient-relevant trial objectives and endpoints.”

We suggest deleting this sentence, as this would be part of the active patient involvement in planning and designing clinical trials.

Line 356 ff:

“Patients’ input can bring value if their insights are proactively included into the planning and design stages of a clinical trial when endpoints, assessments, trial duration, etc. are determined. It may be useful to integrate the perspectives of both recently diagnosed persons, who may know little about the disease, and persons who have lived with the disease for a long time and experienced its different stages, treatments and symptoms. It may also be interesting to obtain insights of people who indirectly live with the disease, such as informal caregivers or therapists interacting regularly with the patients. Patient experts can help determine which trial information is meaningful for patients, e.g. when it comes to the inclusion of endpoints or indicators for quality of life.”

We suggest deleting this section, as this would be part of the active patient involvement in planning and designing clinical trials.

In addition to that, and in line with point no. 1 (better discrimination between mandatory requirements and additional options), we would appreciate to state clear in the document that the involvement of patients or patients' representatives in the lay summary compilation and review is encouraged, but not required (e.g. involvement of patients or patients' representative as one option of involving a lay person).

4. To match the literacy levels of the target audience, the Good Lay Summary Practice suggests using a language in the LS that is understandable at the age of 12. The KKS-Network would like to bring into consideration that at literacy level of the age of 12, essential information will be strongly diluted.

Line 807-809:

*“Efforts should be made to prepare LS which are understandable for the general public as of the **age of 12 years.**”*

Line 993-994:

“The EU Expert Group Recommendation states that a well written LS would normally be accessible by young people from the age of 12 years upwards.”

We therefore suggest in line with point no. 1 (better discrimination between essential requirements and additional options), to state clear in the document that there are no mandatory requirements regarding the literacy level for the LS.

5. Regarding the lay summary languages it is stated in the Good Lay Summary Practice that in multinational trials, to meet the EU CTR requirements, lay summaries need to be provided in the languages of each participating EU member state, which would match the languages of the PIS/ICF. The KKS-Network disagrees with this interpretation of the EU CTR, as this is nowhere stated in the EU CTR.

Line 1107-1109:

“To meet the EU CTR requirements, at a minimum, translations must cover the languages of each EU Member State in which the trial took place which will be equivalent to the languages of the PIS/ICF.”

We suggest describing clearly that the translation of the lay summary into the languages of each participating EU member state is a recommendation by the EU Expert Group, however not laid down in the EU CTR.

Additional points to consider

6. Line 73-75: *“However, the practice of patient involvement in the lay summary process and with the purpose of supporting sponsors’ efforts to better meet **patients’ needs** has not yet been consistently established.”*

We suggest to replace the term “patients’ needs” in this sentence, as there is no consensus about the meaning of “need” in health (Asadi-Lari M, Tamburini M, Gray D. Patients' needs, satisfaction, and health related quality of life: towards a comprehensive model. *Health Qual Life Outcomes*. 2004;2:32. Published 2004 Jun 29. doi:10.1186/1477-7525-2-32).

7. Line 101: *“Patient involvement”*

We suggest explaining the term “Patient involvement” here or to refer to the explanation later in the document.

8. Line 143-144: *“Other terms used elsewhere include, but are not limited to, “Plain Language Summary”, “Trial Results Summary” and “Simple Language Summaries””*

“Trial Results Summary” as a term for LS may be misleading and confusing with respect to the “summary of the results of the clinical trial” according to Art 29 (6) and Art. 37 (4) EU 536/2014. We therefore suggest deleting this term.

9. Line 222-224: The footnote at the end of the sentence does not give any information or explanation on the mentioned deferral, i.e. it does not help understanding the point.

After own research, further information on this topic was found in the following document of the EMA: *Appendix, on disclosure rules, to the “Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014”* (EMA/228383/2015 Endorsed, 2 October 2015) https://www.ema.europa.eu/en/documents/other/appendix-disclosure-rules-functional-specifications-eu-portal-eu-database-be-audited_en.pdf , page 14 and following.

The correctness of the reference should be checked.

10. Line 223-224: *“... after the end of the clinical trial in cases of **non-therapeutic pharmaceutical development trials** (Phase 0 or Phase 1).”*

The term „non-therapeutic pharmaceutical development trial” is unclear, we suggest reconsidering another terminology or more detailed explanation.

11. Line 235: *“LS development approaches may **differ** according to the type of sponsor...”*

We suggest adding an explanation why the approaches may differ (e.g. that there is no mandatory defined approach).

12. Line 243-244: "Trial team members, including the physician and scientific/statistical *experts*,"

We suggest changing the term "physician" to investigator or principal investigator for consistency with EU 536/2014.

13. Line 264-265: "*Sponsors who decide to provide LS beyond **mandatory EU requirements** will need to plan for additional translation costs and/or dissemination costs.*"

We suggest including here the details of the mandatory EU requirements.

14. Line 335-336: "*It is important to bear in mind that involving individual patients in LS discussions does not ensure patient representativeness.*"

We suggest deleting this sentence, as it provides little information; patient representativeness is not required/mentioned in the document.

15. Line 672: Table 3.1

The discrimination between the different competency levels is not defined. We therefore suggest deleting the different levels, leaving just the listing of required competencies.

16. Line 913: Figure 3.2

Circles (on the right) are areas used to represent one-dimensional numbers.

We suggest not to use areas to represent one-dimensional numbers, but bar charts where only the height is varied, and the width is kept constant.

The following is described in 'The Visual Display of Quantitative Information' from Edward Tufte (ISBN-10: 1930824130), page 69ff:

"Another way to confuse data variation with design variation is to use areas to show one-dimensional data"

"Many published efforts using areas to show magnitudes make the elementary mistake of varying both dimensions simultaneously in response to changes in one-dimensional data"

"There are considerable ambiguities in how people perceive a two-dimensional surface and then convert that perception into a one-dimensional number. Changes in physical area on the surface of a graphic do not reliably produce appropriately proportional changes in perceived areas."

This also matches the description in the Good Lay Summary Practice line 906 ff: "*In general, bar graphs are recommended for comparison across groups and pie charts for numerical proportions.*"

17. Line 914: Figure 3.2.

The circle (on the right) for Poland (23%) is bigger than for Denmark (37%).

This needs to be the other way around, however in line with our point no. 15, we suggest not to use areas to represent one-dimensional numbers.

18. Line 1475-1476: The specified hyperlink is no longer current. The version 2.3 of the Q&A document specified here is no longer available. The link currently leads to "Clinical Trials Regulation (EU) No 536/2014 DRAFT Questions & Answers, **Version 2.4, July 2020**".

We suggest updating the reference accordingly.

19. Line 1484-1485: The specified hyperlink is no longer current. The document can be found under the following link: https://www.transceleratebiopharmainc.com/wp-content/uploads/2017/02/Implementation-Recommendations_20Jan17_Final.docx

We suggest updating the hyperlink accordingly